REMARKS

Claims 1 through 4 are pending in the instant application. The Examiner has rejected claims 1 through 4 for statutory type double patenting of the "same invention" under 35 U.S.C. § 101 as claiming the same invention as that of claims 1 through 16 of prior U.S. Patent No. 6,406,715 B1 (Cefali). The Examiner states that the release profiles would inherently be the same in the reference as in the instant application because the formulations are the same.

Double patenting results when the right to exclude granted by a first patent is unjustly extended by the grant of a later issued patent. *In re Van Ornum,* 868 F.2d 937, 214 USPQ 761 (CCPA 1982). Since the doctrine seeks to avoid unjustly extending patent rights at the expense of the public, the focus of any double patenting analysis necessarily must be on the claims in the reference patent and the pending application involved in the analysis. The term "same invention" for statutory double patent analysis means an invention drawn to identical subject matter. *Miller v. Eagle Mfg. Co.,* 151 U.S. 186 (1894); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CDPA 1970); and *In re Ockert,* 245 F.2d 467, 114 USPQ 330 (CCPA 1957). In sum, the relevant question is whether the same invention is being claimed twice.

Applicant respectfully submits that the instant application does not claim the identical subject matter as that claimed in the reference. The Examiner states that the release profiles would inherently be the same in the reference as in the instant application because the formulations are the same. However, the claims of the reference and the instant application are directed to different biopharmaceutical features, which may result from a number of different formulations. Niaspan®, the formulation referenced in the specification of the reference and instant application, is an example of an intermediate release nicotinic acid formulation having the biopharmaceutical features claimed by the reference and the instant application. However, neither the reference nor the instant application claim Niaspan's® release profile nor Niaspan's® formulation.

The claims of the reference are directed to the percent of a specified total dose administered of (i) total nicotinic acid (NA) and nicotinuric acid (NUA) recovered in the urine (also called pathway one metabolites) and (ii) pathway two metabolites of niacin recovered in the urine. The metabolite urine recovery measurements were taken *24 hours after administration* of the total NA dose, (Col. 13; 29-42). Further, the measurements were not taken until the study patient was dosed for several days and had reached steady state (i.e. a state of physiological equilibrium especially in connection with a specified metabolic relation or activity, *Merriam Webster's Medical Desk Dictionary,* (1996 Merriam-Webster,

Inc.), (Col. 13; 24, 42 and 49). The percent urinary metabolites recovered were measured for several different total doses of niacin administered, 1000 mg (claim 1), 1500 mg (claim 2), 2000 mg (claim 9) and 2500 mg (claim 13). Thus, the urinary metabolites recovered are a result of a specific total dose of NA administered, after complete absorption has occurred and steady state reached.

In contrast, the claims of the instant application are directed to (i) the percent absorbed of the total nicotinic acid dose administered and (ii) the three time based phases in which the absorption occurs. Absorption is a function of the rate of release of the active ingredient from the drug formulation and the extent to which the release occurs, *Goodman & Gilman's The Pharmacological Basis of Therapeutic,* Tenth Edition, (2001, The McGraw-Hill Companies, Inc.). To determine the percent absorbed, plasma NA or NAU data was generated from frequent blood sampling following the administration of the formulations, (Col. 8; 26-28). The absorption is claimed in three different time based phases, Phase A, Phase B and Phase C. Phase A constitutes the initial time period with minimal absorption and generally occurs from about 1 to about 4 hours after ingestion with up to 19% of the total NA dose administered being absorbed, Phase B constitutes the subsequent time period with most absorption taking place in this phase and generally occurs from about 4 to about 8 hours after Phase A with about 78% to 100% of the total NA dose administered being absorbed and Phase C constitutes the time when absorption has ended and generally occurs at about 5 to about 9 hours with the remainder, if any, of the NA dose administered being absorbed, (Col. 8; 14-24). The total dose of NA administered is not a limitation in any claim of the instant application. Thus, the percent of absorption is expressed in time phases, occurs well before 24 hours and is not dose specific.

The standard test for double patenting under 35 U.S.C. § 101is whether a claim in the application could be literally infringed without literally infringing a corresponding claim in the patent. Applicant submits that there is no corresponding claim between the reference and the instant application upon which to make an element by element comparison because the urinary metabolites were measured after reaching steady state and 24 hours after administration of the total dose of NA while the plasma samples for measuring absorption were taken at least as early as 1 hour after administration and frequently thereafter and little information is provided after the 9 hours mark since little if any of the NA was absorbed after this period. However, Applicant provides a simplified element by element comparison of claim 1 of the reference to claim 1 of the instant patent.

Claim 1 of the reference reads:

An intermediate release nicotinic acid formulation suitable for oral administration once-a-day as a single dose for treating hyperlipidemia without causing drug-induced hepatotoxicity and (ii) (sic) elevations in uric acid or glucose or both, to levels which would require use of said intermediate release nicotinic acid formulation to be discontinued, said intermediate release nicotinic acid formulation comprising

nicotinic acid and a swelling agent, said intermediate release nicotinic acid formulation having an *in vivo* (sic) urinary metabolite profile resulting from the absorption of the nicotinic acid released from the intermediate release formulation following the oral administration of the nicotinic acid to an individual when the nicotinic acid is dosed at about 1000 mg

(a) nicotinic acid and nicotinuric (sic) acid present in the urine in an amount of from about 4.0% to about 26%, and

(b) Pathway 2 metabolites present in the urine in an amount of from about 74% to about 95%.

Claim 1 (as currently pending) of the instant invention reads:

An intermediate release nicotinic acid formulation in a once per day oral dosage form for treating hyperlipidemia without causing treatment limiting hepatotoxicity and treatment limiting elevations in uric acid or glucose levels or both to a level which would require use of said formulation to be discontinued, said formulation exhibiting an *in vivo* stair-stepped absorption profile when a convoluted plasma curve for nicotinic acid released from said formulation is deconvoluted using a Wagner-Nelson method, wherein the stair-stepped absorption profile is generally characterized by three Phases in which

up to 19% of the nicotinic acid dose administered is absorbed between about 1 and about 4 hours following ingestion at the end of the first phase;

between about 78% and about 100% of the nicotinic acid dose administered is absorbed between about 5 and about 9 hours following ingestion at the end of the second phase; and

between about 86% and about 100% of the nicotinic acid dose is absorbed by about 9 hours following the ingestion during the third phase.

Both claim an intermediate nicotinic acid formulation for treating hyperlipidemia without causing treatment limiting hepatotoxicty or increases in uric acid, glucose or both. The reference requires a formulation with a swelling agent while the instant application doesn't. The instant application requires an *in vivo* stair step absorption profile having three phases while the reference doesn't. The reference requires a total dosage administered of 1000 mg while the instant invention doesn't. The reference measures the percent of pathway one and pathway two urinary metabolites and, as mentioned above, these measurements are taken after steady state is reached and 24 hours after administration of a specific dose of NA while the instant application measures percent absorbed of the dosage of NA administered and these measurements are taken at least as early as 1 hour after ingestion of the does and well within 24 hours after ingestion. Thus, Applicant respectfully submits that claim 1 of the reference can be literally infringed without infringing claim one of the instant application. As a result, the "same invention" is not being claimed twice.

Applicant submits that all pending claims are patently distinct over the reference of record under 35 U.S.C. § 101 for the reasons stated above. As a result of the foregoing remarks, it is respectfully submitted that the present application and all pending claims are now in condition for allowance. Therefore, early passage of the above-identified application for U.S. patent to issuance is earnestly solicited.

Should the Examiner have any questions or require further information or clarification, Applicant respectfully requests that the Examiner contact the undersigned at the information indicated below. No fees are believed to be due at this time. However, please charge any additional fees to our Deposit Account No. 50-2543. As 19 September 2004 fell on a Sunday, this response is considered timely filed.

Respectfully submitted,

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CERTIFICATION UNDER 37 C.F.R., §1.10

I hereby certify that the attached papers are being deposited with the United States Postal service as: Express Mail Post Office to Addressee" Service under 37 C.F.R. §1.10 on 20 September 2004 and is addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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